

INTERNATIONAL R & D MEETING
NORWALK, CONNECTICUT
MAY 17 & 18, 1984
NOTES & ACTIONS

CARDIOCONTIN

This product appears to be in the development stage. The discussion centered on which salt (polygalacturonate, gluconate or the base) would give the most appropriate bioavailability and release pattern.

Send the Canadian quinidine comparative study to International Scientific Exchange.

CODEINE CONTIN

Initial study (KGR) in six men using a 100mg tablet vs 100mg immediate release codeine gave an appropriate serum codeine vs time curve.

A larger study from Biodecision Laboratories is due soon and we should obtain the results through KGR.

Discuss our clinical study plans with International Scientific group.

Determine the formulation and stability data of the tablets we have on hand.

OXYCODONE CONTIN

Ben Oshlak has prepared a prototype batch (using the acrylic release system). Stability testing is underway and the US may (RSS) begin clinical trials.

MORPHINE CONTIN (MST, MS CONTIN)

Joe Horodniak has developed a HPLC morphine assay in which a diatomaceous earth column is used in place of multiple extraction steps. We will ask Dr. Horodniak to participate in the Canadian spiked sample programme.

A sustained release buccal tablet is under development. The buccal tablet may give more rapid absorption and greater bioavailability by virtue of bypassing the liver. The UK has a prototype and the US is planning to develop a formulation for clinical work.

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Deposition Exhibit

Purdue et al. v. Endo et al.
Nos. 00 Civ. 8029 (SHS);
01 Civ. 2109 (SHS); 01 Civ. 8177 (SHS)

DX 608

Trial Exhibit

Purdue et al. v. Endo et al.
Nos. 00 Civ. 8029 (SHS);
01 Civ. 2109 (SHS); 01 Civ. 8177 (SHS)

DX 2194

6/3/02 RLB
CONFIDENTIAL INFORMATION

PURDUE U.
ENDO

C 02362

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INDOMETHACIN CONTIN

Stuart Leslie presented bioavailability (6 patients) and dissolution data in comparison to Indocid-R.

PROGESTERONE CONTIN

A dog study (presented by Ben Oshlak) showed that 99% of the progesterone was found in the lymph (thoracic duct) as apposed to plasma. This is of major consideration for absorption of other nonsoluable drugs when used in the contin system.

The pupose of progesterone contin is largely for use in autoimmune diseases.

UNIPHYL

We should send the Canadian developed dissolution data on the UK and US formulations to International Scientific circulation.

We should calculate Wagner Nelson absorbtion profiles for Phyllocontin and Theo-Dur from our comparative bioavailability studies.

A 600 mg tablet is under development and we will most likely go with the US formulation as at is the identical granulation to our 400 mg tablet.

The rate of invitro dissolution can be increased by using an alcoholic or high pH (13.0 or more) medium. Napp U.K. will be investigating the potential for an inhaler containing a theophylline or aminophylline.

IMMUNE GLOBULINS

We should review a recent issue of the American Journal of Medicine regarding the various indications for immunoglobulin administration.

A general review of the the immunoglobulin market in Canada would be of benefit as we will most assuredly be asked our opinion as to which immunoglobulins we will want to market in the near future.

CALCIUM FLUORIDE AND OSSOPAN

We should review the osteoporosis literature and the claims made by Ayerst for its product Oscal as this entire market will be reviewed at the next meeting.

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One particular question that arose was the benefit of the various types of calcium salts and whether or not the additional cost of non-carbonate salts was justifiable.

DOXYCYCLINE

This product is now marketed by Pfizer. Would we be able to import the drug into Canada and sell it without conflicting with Pfizer's patent?

NICOTINE CONTIN

Ken Rothwell reported that a sustained release nicotine tablet would be of considerable value as an aid to smoking cessation. He reported that habitual smokers maintained a constant plasma nicotine level.

We should review the Nicorette literature and determine the relationship between smoking and plasma nicotine levels.

COMPLEMENT (sustained release vitamin B6)

This product is sold in the UK for OC associated depression. Recent evidence that vitamin B6 is of benefit in the premenstrual syndrome would appear to offer a considerably larger market for this product. It was also reported that zinc improves the efficacy of vitamin B6 in these disorders.

STANDARDIZED BETADINE AND BETADINE SP

We should review the Canadian formulations currently using potassium iodate and send a summary of our experience to International circulation.

The formulation for Betadine vaginal suppositories should be sent to Bill Herlihy.

Stability data on Betadine vaginal suppositories should be sent to Jim Sullivan and Donald Deraska. We should also note if it remains important to protect the suppositories from heat during shipment and storage (ie. will they leak).

John H. Stewart
May 22, 1984

JHS:bs